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THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Alan R. Tall, Carrie L. Welch, and

Chien-Ping Liang

U.S. Serial No. : 09/898,554

Filed : July 2, 2001

For : ATHEROSCLEROSIS SUSCEPTIBILITY GENE

LOCUS 1 (ATHSQ1) AND ATHEROSCLEROSIS

SUSCEPTIBILITY GENE LOCUS 2 (ATHSQ2)

1185 Ave of the Americas New York, New York 10036

October 4, 2001

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

UNDER 37 C.F.R. § 1.97(b) (3)

In accordance with their duty of disclosure under 37 C.F.R. § 1.56, applicants would like to direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (Exhibit 1) and attached hereto as Exhibits 2-23:

- 1. Cominacini L. et al., (2000) Oxidized low density lipoprotein (ox-LDL) binding to ox-LDL receptor-1 in endothelial cells induces the activation of NF-kB through an increased production of intracellular reactive oxygen species. The Journal of Biological Chemistry 275(17):12633-12638 (April 28, 2000) (Exhibit 2);
- 2. Cominacini L. et al. (2001) The binding of oxidized low-density lipoprotein (ox-LDL) to ox-LDL receptor-1 reduces the intracellular concentration of nitric oxide in endothelial cells through an increased production of superoxide. <u>J. Biol. Chem.</u> 276 (17):13750-5 (April 27, 2001); published as Manuscript M010612200 on January 24, 2001 (Exhibit 3);

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- 3. Draude, G., Hrboticky, N. and Lorenz, R.L. (1999) The expression of the lectin-like oxidized low-density lipoprotein receptor (LOX-1) on human vascular smooth muscle cells and monocytes and its down-regulation by lovastatin. Biochemical Pharmacology 57:383-386 (Exhibit 4);
- 4. Draude, G. and Lorenz, R.L. (2000) TGF-β1 downreguates CD36 and scavenger receptor A but upregulates LOX-1 in human macrophages. <u>Am. J. Physiol. Heart Circ. Physiol.</u> 278: H1042-H1048 (Exhibit 5);
- 5. Hoshikawa, H. et al. (1998) High affinity binding of oxidized LDL to mouse lectin-like oxidized LDL receptor (LOX-1). Biochemical and Biophysical Research Communications 245:841-846 (Exhibit 6);
- 6. Kakutani, M. et al. (2000) A platelet-endothelium interaction mediated by lectin-like oxidized low-density lipoprotein receptor-1. Proceedings of the National Academy of Sciences 97: 360-364 (January 4, 2000) (Exhibit 7);
- 7. Kataoka, H. et al., (2000) Biosynthesis and post-translational processing of lectin-like oxidized low density lipoprotein receptor-1 (LOX-1). The Journal of Biological Chemistry 275(9):6573-6579 (March 3, 2000) (Exhibit 8);
- 8. Kume, N. and Kita, T. (2001) Lectin-like oxidized low-density lipopotein receptor-1 (LOX-1) in atherogenesis.

 Trends Cardiovasc. Med. 11:22-25 (Exhibit 9);
- 9. Li, D. and Mehta, J.L. (2000) Antisense to LOX-1 inhibits oxidized LDL-mediated upregulation of monocyte

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chemoattractant protein-1 and monocyte adhesion to human coronary artery endothelial cells," <u>Circulation</u> 101:2889-2895 (Exhibit 10);

- 10. Li, D. et al. (2000) Oxidized LDL upregulates angiotensinII type 1 receptor expression in cultured human coronary artery endothelial cells. The potential role of transcription factor NF-κB. <u>Circulation</u> 102:1970-1976 (Exhibit 11);
- 11. Li, D. et al. (2000) Upregulation of endothelial receptor for oxidized LDL (LOX-1) by oxidized LDL and implications in apoptosis of human coronary artery endothelial cells.

 Evidence from use of antisense LOX-1 mRNA and chemical inhibitors. Arterioscler. Thromb. Vacs. Biol. 20:1116-1122 (Exhibit 12);
- 12. Li, X. et al. (1998) Assignment of the human oxidized low-density liporotein receptor gene (OLR1) to chromosome 12p13.1→p12.3, and identification of a polymorphic CA-repeat marker in the OLR1 gene. Cytogenet Cell Genet 86: 34-36 (Exhibit 13);
- 13. Minami, M. et al. (2000) Transforming Growth Factor- β_1 increases the expression of lectin-like oxidized low-density lipoprotein receptor-1. Biochemical and Biophysical Research Communications 272:357-361 (Exhibit 14);
- 14. Morikawa, H. et al. (1998) Expression of lectin-like oxidized low density lipoprotein receptor-1 in human and murine macrophages: upregulated exression by TNF-~,"

 Federation of European Biochemical Societies 440: 29-32 (Exhibit 15);
- 15. Murase, T. et al. (2000) Identification of soluble forms of

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lectin-like oxidized LDL receptor-1. <u>Arterioscler Thromb</u> <u>Vasc. Biol.</u> 20: 715-720 (Exhibit 16);

- 16. Nagase, M. et al. (1998) Genomic organization and regulation of expression of the lectin-like oxidized low-density lipoprotein receptor (LOX-1) gene. The Journal of Biological Chemistry 273(50): 33702-33707 (Exhibit 17);
- 17. Nagase, M. et al, (1998) Unique repetitive sequence and unexpected regulation of expression of rat endothelial receptor for oxidized low-density lipoprotein (LOX-1).

 Biochem. J. 330: 1417-1422 (Exhibit 18);
- 18. Nagase, M: et al. (2000) Expression of LOX-1, an oxidized low-density lipoprotein receptor, in experimental hypertensive glomerulosclerisis. J. Am. Soc. Nephrol. 11:1826-1836 (Exhibit 19);
- 19. Renedo, M. et al. (2000) A sequence-ready physical map of the region containing the human natural killer gene complex on chromosome 12p12.3-p13.2. Genomics 65: 129-136 (Exhibit 20);
- 20. Sawamura, T. et al. (1997) An endothelial receptor for oxidized low-density liporotein. Nature 386: 73-77 (Exhibit 21);
- 21. Yamanaka, S. et al. (1998) The human gene encoding the lectin-type oxidized LDL receptor (OLR1) is a novel member of the natural killer gene complex with a unique expression profile. Genomics 54: 191-199 (Exhibit 22); and
- 22. Li, X., Bouzyk, M.M., and Wang, X.K. (1998) Human oxidized low density lipoprotein receptor: characterization of the full length cDNA sequence and assignment to human

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chromosome 12p13.1-12.3. GenBank Accession No. AF035776, published December 2, 1998 (Exhibit 23).

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Applicants are filing this Information Disclosure Statement under 37 C.F.R. §1.97(b)(3) before the mailing of a first Office Action on the merits. Accordingly, no fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

certify that this hereby correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

hn P. White

Reg. No. 28,678

John P White Registration No. 28,678 Attorney for Applicants Cooper & Dunham LLP 1185 Avenue of the Americas New York, New York 10036 (212) 278-0400